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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,905	09/23/2004	Reddy Bandi Parthasaradhi	H1089/20012	8361
3000 7590 04/23/2007 CAESAR, RIVISE, BERNSTEIN, COHEN & POKOTILOW, LTD. 11TH FLOOR, SEVEN PENN CENTER 1635 MARKET STREET PHILADELPHIA, PA 19103-2212			EXAMINER SHIAO, REI TSANG	
			ART UNIT	PAPER NUMBER
			1626	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		04/23/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

**Office Action Summary**

Application No.

10/508,905

Applicant(s)

PARTHASARADHI ET AL.

Examiner

Rei-tsang Shiao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 March 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 5-14 and 17-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 15 and 16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 September 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>08/15/05, 2/18/05</u> | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Claims 1-19 are pending in the application.

#### ***Information Disclosure Statement***

2. Applicant's Information Disclosure Statements, filed on August 15, 2005 and February 18, 2005 have been considered. Please refer to Applicant's copies of the 1449's submitted herein.

#### ***Responses to Election/Restriction***

3. Applicant's election with traverse of Group I claims 1-4 and 15-16, in part, in the reply filed on March 07, 2007, is acknowledged. The traversal is on the ground(s) that the special technical feature which links the claimed inventions is the structure of the compounds which is not taught by US 2005/0106236. This is found not persuasive, and the reasons are given *infra*.

Claims 1-19 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 1- 4 and 15-16, in part, drawn to a crystalline Form I of a compound/composition of tegaserod maleate, and their processes of making.

The claims 1-19 herein lack unity of invention under PCT rule 13.1 and 13.2 since the compounds defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art, see Aubert et al. US 2005/0106236 A1. Aubert et al. do disclose the instant compound of tegaserod maleate and its pharmaceutical composition, see columns 1-2.

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Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper.

Furthermore, even if unity of invention under 37 CFR 1.475(a) is not lacking, which it is lacking, under 37 CFR 1.475(b) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations:

- (1) A product and a process specially adapted for the manufacture of said product', or
- (2) A product and a process of use of said product; or
- (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
- (4) A process and an apparatus or means specifically designed for carrying out the said process; or
- (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

And, according to 37 CFR 1.475(c)

if an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b), unity of invention might not be present.

However, it is noted that unity of invention is considered lacking under 37 CFR 1.475(a) and (b). Therefore, since the claims are drawn to more than a product, and according to 37 CFR 1.475 (e)

the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

The claims lack unity of invention and should be limited to only a product, or a process for the preparation, or a use of the said product. In the instant case, Groups I-IV are drawn to various products, processes of making, and the final products do not

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contain a common technical feature or structure, and do not define a contribution over the prior art, i.e., a crystalline form I of claims 1-4, a crystalline form II of claims 5-7, a crystalline form III of claims 8-11 and a crystalline form IV of claims 12-15. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner. Claims 1-4 and 15-16 are prosecuted in the case. Claims 5-14 and 17-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2, line 2, respectively recites the limitation "figure 1" fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims must stand alone to define invention, and incorporation into claims by express reference to specification is not permitted, are properly rejected under 35 U.S.C. 112, second paragraph, see *Ex parte Fressola*, No. 93-0828. Incorporation of the X-ray powder diffraction data into claim 2, would obviate the rejection.

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Claim 15 recite the limitation "a crystalline form of tegasaerod maleate", is indefinite and ambiguous. It is unclear which crystalline forms are in the composition. Is it form I, form II or form III? Clarification is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is well recognized in the art that process of preparing pharmaceutical composition will produce the thermodynamically stable form of crystals, thus, the instant Form III, after mixing, grinding, compressing would be transformed into a thermodynamically stable form(s), see Brittain's publication, pages 348-361.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,

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5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case:

**The nature of the invention**

The nature of the invention is a pharmaceutical composition comprising a crystalline form of tegaserod maleate.

**The state of the prior art and the predictability or lack thereof in the art**

The state of the prior art is that a similar pharmaceutical composition comprising tegaserod maleate. see columns 1-4 of Aubert et al. US 2005/0106236 A1.

**The amount of direction or guidance present and the presence or absence of working examples**

The only direction or guidance present in the instant specification is the general description of the instant pharmaceutical composition on pages 2-4. There is no data present in the instant specification for the instant solid pharmaceutical composition, wherein the crystalline form I still exists after the process of preparation, i.e., mixing, grinding, and compressing.

**The breadth of the claims**

The instant breadth of the rejected claims lack enablement requirement, specifically, the instant solid pharmaceutical composition comprises the crystalline form I after processes of preparing pharmaceutical compositions.

***The quantity or experimentation needed and the level of skill in the art***

While the level of the skill in the chemical arts is high, it would require undue experimentation of one of ordinary skill in the art to resolve any solid pharmaceutical compositions, wherein the crystalline form I still exist after the processes of pharmaceutical preparation. There is no data present in the instant specification for the instant solid pharmaceutical compositions, wherein the crystalline form I still exist after the process of preparation, i.e., mixing, grinding, and compressing. Therefore, the claims lack enablement for the pharmaceutical composition comprising the crystalline form I.

***Prior Art Rejections***

6. In regards to applicants compound claims 1-11 and 19, the prior art references of Aubert et al. US 2005/0106236 A1, while not providing applicants' instant X-ray diffraction data. However, Aubert et al. do name the instant compound tegasaerod maleate, see working columns 1-4, which puts this product in the public domain. As these forms differ from the claims in that the references are silent on the X-ray diffraction data or the crystalline form, applicants must show that their crystalline form really is different from any of the ones prepared in the prior art. MPEP 2112 states:



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"Something which is old does not become patentable upon the discovery of a new property. The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In this case, the 'unknown property' is the particular crystalline form. This is unknown because the references are silent on this property. MPEP 2112 goes on to state: "A rejection under 35 USC 102/103 can be made when the prior art product seems to be identical except that the prior art is silent as to an inherent characteristic. Where applicant claims a composition in terms of a function, property or characteristic and the compositions of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 USC 102 and 103, expressed as a 102/103 rejection." Again, the "characteristic" which the prior art is silent on is the crystalline form or the X-ray diffraction data.

This is not an ordinary inherency situation where it is not explicitly stated what the product actually is. Here the reference explicitly teaches exactly what the compound is. The only difference is a characteristic about which the reference happens to be silent. See also Ex parte Anderson, 21 USPQ 2d 1241 and 1251, discussion of Rejection E. There, the decision states, "There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture." (page 1253). The "properties' branch of that statement applies here. Applicants are reminded that the PTO has no testing facilities. The composition claims

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15-16 are rejected under 35 USC 102(a) or (e) as the prior art references disclose compositions comprising applicants' instantly claimed invention as it is the state of the prior art that the preparation of pharmaceutical compositions requires, milling, adding excipients, surfactants, etc. The process of preparing a pharmaceutical composition will cause a specific crystalline form, if in the metastable state, to resort back to the most thermodynamically stable form, which is the form with the lowest vapor pressure.

Polymorphs tend to convert from less stable to more stable forms, see

Brittain's publication, polymorphism in Pharmaceutical Solids, Drugs and the Pharmaceutical Science; 1999, V. 95, pages 348-361.

### ***Claim Rejections - 35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1-4 and 15-16 are rejected under 35 U.S.C. 102(a) or 102(e) as being anticipated by Aubert et al. US 2005/0106236 A1. Aubert et al. '236 is 102 (e) reference.

Applicants claim a compound and its pharmaceutical composition comprising tegasaerod maleate, see claim 1 and 16.

Aubert et al. discloses the same instant compound and its a pharmaceutical composition comprising a compound tegasaerod maleate, see columns 1-4. It is noted that a crystalline form of a compound is an innate nature of a solid compound. Therefore, the instant compound and its pharmaceutical composition are anticipated by Aubert et al.

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-4 and 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aubert et al. US 2005/0106236 A1 in view of Brittain's publication, polymorphism in Pharmaceutical Solids, Drugs and the Pharmaceutical Science; 1999, V. 95, pages 348-361. Aubert et al. '236 is 102 (e) reference.

Applicants claim a compound and its pharmaceutical composition comprising a compound tegasaerod maleate, see claim 1 and 16.

**Determination of the scope and content of the prior art (MPEP §2141.01)**

Aubert et al. discloses the same instant compound and its a pharmaceutical composition comprising a compound tegasaerod maleate (solid form), see columns 1-4. It is noted that a crystalline form of a compound is an innate nature of a solid compound.

**Determination of the difference between the prior art and the claims (MPEP §2141.02)**

The difference between the instant claims and Aubert et al. is that Aubert et al. is silent on the X-ray diffraction data of the instant compound.

Moreover, it is well recognized in the art that process of preparing pharma-

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ceutical composition will produce the thermodynamically stable form of crystals, thus, Aubert et al. solid form and the instant form I after mixing, grinding, compressing would both be transformed into the same thermodynamically stable form(s) of the instant compound, see Brittain's publication, pages 348-361.

**Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)**

One having ordinary skill in the art would find the instant claims 1-4 and 15-16 prima facie obvious **because** one would be motivated to employ the compounds/compositions of Aubert et al. to obtain the instant crystalline or solid form of the same compound tegasaerod maleate and its pharmaceutical compositions. Further, changing the form, purity or other characteristic of an old product does not render the novel form patentable where the difference in form, purity or characteristic was inherent in or rendered obvious by the prior art, see *In re Cofer*, 148 U.S.P.Q. 268 (CCPA 1966). Therefore, absent a showing of unobvious and superior properties in terms of mechanic benefits, the instant claimed crystalline forms and its compositions of known compounds would have been suggested to one skilled in the art.

The motivation to obtain the claimed crystalline form of the compound tegasaerod maleate or its pharmaceutical composition derives from known Aubert et al. pharmaceutically useful compounds/compositions with the expectation of obtaining a pharmaceutically useful benefit, such as longer shelf life, stability, enhanced deliverability, etc., would possess similar activities (i.e., agents treating disease) to that which is claimed in the reference.

### ***Claim Objections***

**10.** Claims 15-16 are objected. Since claim 15 or 16 is independently drawn to a solid pharmaceutical composition, amendment of claim 15 or 16 as a solid pharmaceutical composition claim would obviate the objection.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rei-tsang Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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A handwritten signature in black ink, appearing to read 'Rei-tsang Shiao'.

Rei-tsang Shiao, Ph.D.  
Patent Examiner  
Art Unit 1626

April 17, 2007